THE CEREBROSPINAL FLUID IN POLIOMYELITIS

WITH ESPECIAL REFERENCE TO THE LANGE REACTION *

P. C. JEANS, M.D., AND MEREDITH R. JOHNSTON, M.D.
ST. LOUIS

Early in poliomyelitis, before the onset of paralysis, or in those abortive cases which do not develop paralysis, there is found no pathognomonic diagnostic feature either at the bedside or in the laboratory. The clinical picture and history are usually fairly uniform and striking, but these same symptoms and signs are of such frequency in other infections that a reliable diagnosis cannot be made from them alone. The nearest evidence of a positive nature as to the presence of this infection in a preparalytic or abortive case is secured by the correlation of the clinical data with the results of examination of the cerebrospinal fluid.

The characteristics of cerebrospinal fluid in the early stages of poliomyelitis will be briefly summarized. It is clear and increased in amount. From 15 to 60 c.c. or more may be readily withdrawn. It frequently shows a marked web formation. The reduction of Fehling's solution is prompt, as in a normal fluid. There is a slight to moderate increase in the albumin, globulin and cellular elements. The cell counts vary from practically normal in a few cases to 500 or more per cubic millimeter, the majority having less than 200 cells per cubic millimeter. Eighty per cent. or more of these cells are mononuclears.

There are three rare types of cerebrospinal fluid found. One of these is a slightly cloudy fluid which shows a polymorphonucleosis, usually about 60 per cent., but which may be as high as 90 per cent. The other two types occur when the hemorrhagic process has been more than usually extensive. One of these has blood evenly diffused throughout the fluid, and the other, though having no blood cells, has a yellow color and coagulates spontaneously. The latter type has recently been present in our St. Louis material.

Conditions which may be confused with preparalytic or abortive poliomyelitis are *meningism, syphilis* and meningitis, either *tuberculous* or *purulent.*

In meningism is found a fluid increased in amount but normal in character, and the underlying infection is usually manifest after a short interval, if not at the first examination.

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* From Department of Pediatrics, Washington University Medical School, St. Louis, and the Research Laboratory of the Department of Health of the City of New York.

In syphilis of the central nervous system there is usually found a fluid identical with that of poliomyelitis. However, in syphilis the fluid gives a positive Wassermann reaction and there is rarely if ever an acute onset with fever in children.

In purulent meningitis, even in the early stages, there is usually some degree of cloudiness from cellular increase and the cells are 90 per cent. or more polymorphonuclears. In certain mild cases of the epidemic variety the organism may never appear, but in the other varieties it will practically always appear, if not present at the first examination, as further punctures are made.

The differential diagnosis of poliomyelitis from tuberculous meningitis will often present difficulties. In both conditions the fluid is usually clear. The increase in the albumin, globulin and the cellular elements is usually greater in tuberculous meningitis than in poliomyelitis. The reduction of Fehling's solution is usually better in poliomyelitis, though many fluids from tuberculous meningitis reduce Fehling's solution readily, especially if obtained early in the disease. In both conditions there is usually mononucleosis, although in some cases of tuberculous meningitis there is a polymorphonucleosis. By careful search, tubercle bacilli may be found in 90 per cent. or more of fluids from tuberculous meningitis. In the remaining cases, animal inoculation and the clinical course of the disease must be depended on. Tuberculous meningitis seldom has the acute onset and high fever that accompany poliomyelitis. By correlating the laboratory findings with the clinical picture the differential diagnosis is usually not difficult, though several cases are recalled in which the diagnosis was later proved to be in error.

Since there is no one laboratory measure that is pathognomonic of this disease, it seems advisable to extend the laboratory examination as much as would prove helpful in arriving at a definite diagnosis. The Lange colloidal gold reaction has been observed by one of us on a small number of fluids from patients in cases of poliomyelitis occurring sporadically in St. Louis.[1] In these cases the occurrence of an early transitory reaction in the "syphilitic zone" in the acute stage suggested an important aid in the diagnosis. In order to study the reaction in a larger number of cases, Lange colloidal gold tests were made with fluids from patients in 100 cases occurring in the 1916 New York epidemic (Table 1).

Fifty-five of these patients had symptoms, including paralysis, which were sufficient evidence that they had poliomyelitis. In the fluids from the entire fifty-five there was definite reduction of the colloidal

1. Johnston, M. R.: A Study of Normal and Pathologic Cerebrospinal Fluids in Children, AM. JOUR. DIS. CHILD., 1916, **12,** 112.

gold solution with the lower dilutions of spinal fluid. This reaction occurred in a fairly uniform and regular manner, just as had happened previously in a smaller number of sporadic cases in St. Louis. In seven of these cases the Noguchi test gave a doubtful result (±) for globulin. In five of the seven there was no increase, or only very slight increase, in the cells. So that even in those cases of undoubted poliomyelitis in which there was apparently no change in the spinal fluid as far as the usual methods of examination show, the Lange test showed definite changes and was the only good evidence, aside from paralysis, that the cases were poliomyelitis.

The number of cases seen without paralysis, but which later developed paralysis, is not definitely known, but several are known to have progressed in this manner following the first lumbar puncture at which the material for this study was obtained, and in these cases the colloidal gold reaction was essentially no different in the pre-paralytic stage from that obtained after paralysis had developed.

Abortive cases which never become paralyzed are known to occur with considerable frequency. With the usual symptoms of onset and a cerebrospinal fluid that presents increased globulin and cells, a diagnosis of poliomyelitis is justified even in the absence of paralysis. In all such cases in this study the colloidal gold reaction was similar to that of the paralytic cases.

In cases presenting the usual symptoms of onset, not developing paralysis, and in which the cerebrospinal fluid showed no increase in the globulin, and slight or no increase in cells, but causing the usual colloidal gold reaction, it is to be concluded that these were cases of abortive poliomyelitis. It is in such cases that the Lange reaction shows its greatest usefulness. In this small series there were four such cases and two others having an increase in cells, but a doubtful globulin test. A Lange reaction is good evidence that a spinal fluid is pathologic and is sufficient to differentiate between poliomyelitis and meningismus or any other condition giving a normal cerebrospinal fluid.

The occasional difficulty of differentiating between a fluid from poliomyelitis and one from tuberculous meningitis is not made absolutely conclusive by the colloidal gold reaction. As is seen in the accompanying table (Table 2), fluids from cases of tuberculous meningitis cause the greatest changes in the middle dilutions, while the greatest changes caused by a fluid from poliomyelitis are in the lower dilutions. A distinct limitation of the maximum intensity to these zones is not constant in either condition. However, fluids from cases of poliomyelitis which cause a maximum change in the "Middle zone" at the same time produce changes in the lower dilutions — which is not the case with fluids from tuberculous meningitis. The variations in these reactions are so rare that we believe the colloidal gold reaction is

TABLE 1.—Results of Examination of Cerebrospinal Fluid in 100 Cases of Poliomyelitis *

No.	Lange Reaction	Albumin	Globulin (Noguchi)	Sugar (Fehling)	Cellular Increase†	Mononuclear, %	Amt., C.c.	Age, Years	Day of Disease	Remarks
2570	1112331000	++	+ 1	+++	Gt.	98	20	25	4	Paralysis of both lower extremities
2571	1123310000	++	++	+++	Mod.	70	10	32	4	Paralysis of left quadriceps and right leg
2573	1112200000	++	++	+++	No	..	35	5	19	Temperature 101 on day of admission, 14 days after onset; no paralysis
2791	1122210000	+	+ 1	+++	Sl.	100	..	5	30	
2574	1124300000	++	+ 1	+++	No	98	40	4	9	No paralysis; tenderness over spine; rigidity of back; temperature normal
2575	1122110000	+	±	+++	Sl.	98	30	4	13	No paralysis; temperature normal
2600	1221000000	+ 1	+ 1	+++	Sl.	95	25	Infant	8	Weakness of muscles of shoulder, neck and back on right side
2760	1232120000	+ 1	++ 1	+++	Sl.	100	15	..	17	
2601	1122110000	+ 1	++	+++	Sl.	95	25	3	8	Paralysis of right upper and both lower extremities; temperature normal
2602	1122200000	++	+ 1	+++	Mod.	98	25	..	13	Paralysis left deltoid; rigidity of neck
2610	1112100012	++	++	+++	Mod.	..	25	3	12	Temperature normal at time of puncture; no paralysis; had a general tremor
2762	1233110000	+	+	+++	Sl.	100	10	..	21	
2611	1221100000	++ 1	++ 1	+++	Mod.	90	30	2½	13	Temperature slightly elevated; Kernig and Macewen signs elicited; paralysis of left leg
2765	1112220000	+ 1	++	+++	Sl.	..	15	..	22	
2612	1122110000	++ 1	++ 1	+++	Sl.	..	10	2	12	Temperature normal; weakness of left quadriceps extensor
2764	1123331000	+ 1	++	+++	Mod.	100	12	..	21	
2614 ‡	1122100000	++	+	+	Mod.	90	..	1½	7	Child had never walked; had general weakness of long standing; hyperesthesia and general irritability at onset; high temperature on third and fourth days; no rigidity; Macewen sign doubtful; no paralysis
2615	1122210000	+	+	+++	Gt.	98	30	3	4	No paralysis; delirious; Macewen sign; tenderness along spine
2617	1112100000	++	++	+++	Gt.	98	12	6	6	No paralysis; temperature normal; clinically diagnosed "no case"
2780	1123210000	++	++	+++	Mod.	100	20	..	15	
2618	1123210000	++	+ 1	+++	Mod.	98	35	4	6	No paralysis; slight fever; weakness right leg 4 days later
2619	1123310000	+ 1	+ 1	+++	Gt.	99	15	3	9	Clinically diagnosed tuberculous meningitis; later appeared weakness of right shoulder; recovered
2623	1111000000	+	+	+++	Mod.	95	25	6½	4	Double ptosis; eye movements not coordinate; unable to swallow; weakness left deltoid, neck and back; diaphragmatic respiration. Died on fourth day
2625	1123210000	+ 1	+ 1	+++	Gt.	90	25	2½	3	Temperature 102; paralysis of both upper and lower extremities
2626	1123321000	+ 1	+ 1	++	Gt.	95	25	2	3	Paralysis of back, both deltoids and both lower extremities
2628	1122210000	+ 1	+ 1	++	Mod.	90	12	3	4	Died same day; diaphragmatic paralysis
2630	1123321000	+ 1	+	+	Mod.	95	12	6	7	Temperature normal; weak right arm and weak neck
2631	1121000000	+	±	+++	Sl.	90	25	1	8	Temperature 101; weak neck, back and deltoids; paralysis of quadriceps

2632	1123300000	+ 1	+ 1	+++	Mod.	90	18	1½	1	Temperature 103; developed paralysis of both legs
2633	0111100000	++	++	+++	Gt.	90	15	1½§	..	Paralysis both arms and legs, neck, back and right facial. Died third day
2634	1121000000	+	+	+	Gt.	90	12	4	3	Temperature 101; paralysis of left deltoid
2636	1122210000	++	+++	+++	Sl.	90	15	¾	2	Weak neck and back; paralysis of both legs
2639	0112210000	++	+ 1	+++	No	..	30	28	6	Temperature 100; previously higher; drowsiness; general weakness, especially of back; Wassermann reaction negative; clinical diagnosis, hysteria; five days later had Rombergism and weakness of right facial
2640	1122100000	+	+	+++	Sl.	90	15	..	..	Died; no paralysis; question of tuberculous meningitis
2641	1111000000	+	±	+++	Sl.	..	25	1½	4	No paralysis; onset with headache, vomiting, temperature 103; at time of puncture temperature 100, hyperesthesia, rigidity of neck; Macewen sign; tenderness over spine
2644	1121000000	+++	+++	+++	Mod.	95	12	3	4	No paralysis; onset sudden with temperature 103, headache and apathy; at time of puncture temperature 98.2; hyperesthesia; irritable; rigidity of neck; Macewen and Kernig signs elicited
2645	1122100000	+ 1	+ 1	+++	Gt.	90	35	2	2	No paralysis; onset with temperature 105; vomited once; at time of puncture slight rigidity of neck; hyperesthesia, tenderness over spine; Macewen
2646	1111000000	+	+	+++	Gt.	40	20	9	2	No paralysis; onset with temperature 103; vomiting and apathy; at time of puncture temperature 102; hyperesthesia; rigidity of neck; Macewen and Kernig signs positive
2647	1122100000	+	+	++	Mod.	95	20	3	6	Temperature 102.4; rigidity of neck and back; weak quadriceps; later thoracic paralysis
2648	1111000000	+	+	++ 1	Sl.	90	13	2	5	Paralysis left deltoid and both legs; later died of respiratory paralysis
2649	1122100000	+ 1	+ 1	++	Mod.	90	20	..	3	Paralysis both deltoids and quadriceps; temperature 101 to 104; later intercostal paralysis
2652	1121000000	+	+	++	Gt.	98	30	7	..	Probably poliomyelitis; no paralysis
2653	1111000000	+	±	+++	Mod.	90	30	2	..	Probably poliomyelitis; no paralysis
2654	2231000000	±	±	++	Sl.	95	10	2	5	Probably poliomyelitis; no paralysis; temperature normal
2655	1111100000	+	+	++	Mod.	98	..	6	3	Paralysis without previous illness
2661	1123110000	+	+	+++	Gt.	98	50	8½	5	Paralysis flexors left arm; rigidity neck and back; pain back and legs
2662	1121000000	+	+	+++	Gt.	95	..	7	1	No paralysis; fever, headache, vomiting; rigidity of neck
2664	1122110000	++	++	+++	Mod.	98	15	1½	7	Paralysis of right leg; temperature normal
2667	1111000000	+	+	+++	Sl.	95	25	2	16	Left facial paralysis; temperature normal; later right deltoid paralysis
2668	0125533510	++	++	+++	Gt.	99	20	2	2	Fever, stupor, tenderness over spine; later paralysis right leg and both arms
2669	1123332000	++	++ 1	+++	Gt.	98	..	5	3	Onset with temperature 103; vomiting and headache; rigidity of neck; temperature 101.2; partial paralysis both legs; irritable
2724	0123210000	+++	+++	++	No	..	..	..	6	
2677	2233310000	+++	++ 1	+++	Mod.	99	18	5	5	Temperature slightly elevated; paralysis of left leg

* For the nonparalytic cases in which information was obtainable there is appended a brief of the clinical data.

† The abbreviations denoting cellular increase indicate as follows: Sl. = slight increase, i. e., from 10 to 50 per c.mm.; Mod = moderate increase, i. e., from 50 to 150 per c.mm.; Gt. = great increase, i. e., above 150 per c.mm.

‡ 2614. Fluid from previous puncture bloody. This specimen shows a few red blood cells.

§ 2633. Age 1½ months.

TABLE 1.—RESULTS OF EXAMINATION OF CEREBROSPINAL FLUID IN 100 CASES OF POLIOMYELITIS *—(*Continued*)

No.	Lange Reaction	Albumin	Globulin (Noguchi)	Sugar (Fehling)	Cellular Increase†	Mononuclear, %	Amt., C.c.	Age, Years	Day of Disease	Remarks
2678	1122100000	+	±	++	Sl.	100	7	2	2	Temperature 102; rigidity of neck and back; right facial paralysis
2679	2333233100	++ 1	++	+++	No	..	18	5/6	3	Temperature 101; paralysis both legs and left arm; died fifth day of respiratory paralysis
2680	1234310000	++	++	+++	Sl.	100	30	4½	2	Temperature normal; no paralysis; rigidity of neck and back; opisthotonus
2681	0112333111	+++	+++	+++	No	..	35	2	..	Rigidity neck and back; paralysis quadriceps and intercostals; died ninth day
2682	2333311000	+	+	+++	Mod.	100	35	3½	3	Onset with vomiting and temperature 102; left facial paralysis; Kernig; rigid neck
2683	1111100000	+ 1	+ 1	+++	Sl.	..	..	12	..	Clinical diagnosis, meningeal irritation due to injury; observed and punctured 8/16/16; had a fall 7/4/16; improved to two weeks ago when he began to feel bad again; much worse past few days; stuporous; Macewen and Kernig; clonus right ankle; on 10/14/16 report of complete recovery
2685	1112321000	++ 1	++ 1	+++	Mod.	95	35	1	7	Onset with gastro-enteritis; fever and prostration since; comatose; died seventh day of "respiratory paralysis"
2689	1122100000	+	+	++	Gt.	99	25	3¾	..	Paralysis both arms, legs, neck, voice and respiration; died sixth day
2695	1121100000	+	±	+++	Sl.	90	..	2⅔	3	Irritable; hyperesthesia; Macewen; questionable weakness right leg; (onset with temp. 103; headache, vomiting and apathy)
2696	1122200000	+	+	++	Mod.	98	..	2½	6	Temp. 102; hyperesthesia; increased reflexes; rigidity of neck; Kernig and Macewen positive; no paralysis; sudden onset with fever
2697	1112110000	+ 1	+ 1	++	Gt.	95	25	..	..	Clonic convulsions; probably poliomyelitis
2698	1222200000	++	+ 1	+++	Gt.	98	30	1½	7	No paralysis; temperature normal; neck rigid; Macewen positive; tenderness over spine; (sudden onset with temp. 103.5)
2703	1122110000	+	+	+++	Mod.	50	25	..	5	Paralysis; Macewen positive; died day of puncture
2704	1123220000	+	+	+++	Mod.	99	20	..	4	Moribund at time of puncture; died of respiratory paralysis
2705	1122210000	+	+ 1	+++	Sl.	98	15	..	4	Paralysis; died
2706	1122100000	+	+	+++	Gt.	100	20	..	8	Moribund; paralysis; died
2708	1122220000	+	+	+++	Mod.	100	15	..	3	Moribund at time of puncture; Macewen positive; reflexes absent; died
2715	±112330000	++	+++	+++	Mod.	100	..	..	2	Continued high fever; no paralysis; comatose; neck rigid; Kernig and Macewen positive; history of pertussis for two weeks; clinical diagnosis of tuberculous meningitis had been made; no tubercle bacilli found in fluid; died few hours after puncture
2717	1122100000	+	+	+++	Sl.	98	25	⅔	4	Temperature 101; paralysis of both legs
2718	1112331000	+	+	+++	Gt.	99	20	⅛	3	Temperature 100; rigidity of neck and back; question of anterior tibial paralysis
2720	1112331000	+++	++	+++	Sl.	100	12	¼	3	Died; paralysis respiratory muscles and of both arms and legs
2723	1233200000	+	+	+++	Mod.	99	30	3½	4	Fever; no paralysis; tremors and slight spasticity left leg
2725	1123331000	++	++	+++	Mod.	100	12	Adult	7	Paralysis of both legs
2729	1232200000	+	+	+++	Sl.	100	30	5	7	Temperature 99; left facial paralysis

2730	1133310000	+ 1	+ 1	+++	No	..	25	1¼	9	Paralysis left deltoid; (sediment shows slight blood)
2733	1123210000	++ 1	++ 1	+++	Gt.	98	40	13	5	Temperature 101; no paralysis; improving
2734	1122210000	+++	+++	+++	Sl.	100	40	8	21	Temperature 102 on third day; now stuporous; weakness right leg and right side of face
2738	1110000000	+	+	+++	No	100	30	..	..	No paralysis; question of poliomyelitis; had malaria
2740	0132200000	++	++	++	Gt.	100	20	8½	5	Onset with vomiting, headache and fever; temperature now 102; hyperesthesia; difficulty in swallowing; Macewen and Kernig signs positive
2741	1112100000	+	+	+++	Mod.	98	20	..	4	No paralysis; temperature 98.2; apathy; Macewen; rigidity of neck; onset with vomiting, headache and temperature to 102
2755	1233210000	+ 1	+ 1	+++	Gt.	100	25	10	1	Temperature 105; bulbar paralysis; delirium
2769	1122100000	+	±	+++	Gt.	100	25	..	4	Illness followed fall from window to floor; fall at 6:30 p. m.; vomiting in the night; fever next morning, with rigidity of neck and positive Kernig; increased reflexes; no paralysis
2770	1112210000	+++	+++	+++	Sl.	100	25	..	24	Paralysis of left arm and both legs
2771	1112320000	++	+ 1	+++	Sl.	100	15	23	43	Had facial paralysis for one day
2772	1232210000	+	+	++	Mod.	98	30	2	47	Paralysis of both legs; practically well
2773	1123100000	+	±	+++	Mod.	..	40	4	42	Full recovery; had weakness right leg and rigidity of neck and back
2774	1232210000	+	+	+++	Sl.	100	40	5	..	Paralysis left thigh, weakness of right; slight left foot drop; (discharged well eighth week)
2775	1111100000	+	+	+++	Mod.	..	10	6	47	Paralysis, left facial; tremors left thigh and both hands; complete recovery
2776	1123310000	+	+	+++	Mod.	100	..	..	11	Questionable poliomyelitis clinically; had chorea
2777	1122110000	+	+	+++	Gt.	100	20	..	..	Early cases at Queensborough Hospital; paralytic
2778	1123310000	++ 1	++ 1	+++	Mod.	100	18	..	..	
2779	2223110000	+	+	+++	Mod.	95	20	..	..	
2787	1112200000	+ 1	+	+++	Mod.	98	15	1	6	Temperature 100.8; no paralysis; Macewen positive; onset with vomiting and temperature 102
2788	1111000000	+	+	+++	Mod.	100	25	2	2	Temperature 100.8; no paralysis; Macewen positive tender spine; temperature at onset 104
2792	1132210000	+	±	+++	No	..	50	..	12	Paralysis of left leg
2793	1111100000	+	+ 1	+++	Gt.	98	30	..	..	Doubtful diagnosis clinically; question of typhoid
2794	1122200000	++	+	+++	Gt.	100	20	7	3	No paralysis; rigid neck; onset with vomiting, headache and temperature 104
2795	1123210000	++	++	+++	Mod.	99	50	1	4	Rigidity of neck; strabismus; Macewen; onset with vomiting and fever
2796	1112221000	++	++	+++	Mod.	99	40	4	4	No paralysis; irritable; hyperesthesia; rigid neck; tender spine; Macewen and Kernig positive; onset with vomiting and fever
360	1122100000	±	±	+++	No	..	25	..	2	Paralysis present
386	1121100000	+	+	+++	Sl.	98	10	..	2	No paralysis; (later had weakness of legs)
391	1112100000	+	+	+++	Sl.	98	25	..	4	Paralysis of right arm and leg
396	1233100000	+	+	+++	Mod.	97	15	..	17	Left facial paralysis
401	±112100000	+	±	+++	Mod.	98	..	..	17	Paralysis present

a distinct aid in the differentiation of these two conditions, before the clinical picture is entirely clear.

Products in the cerebrospinal fluid of a purulent process in the brain or meninges cause colloidal gold changes in the higher dilutions, thus being quite different from the changes produced by a fluid from poliomyelitis. The other cerebrospinal fluid changes resulting from the various purulent infections, however, are usually such that a Lange test is quite unnecessary.

TABLE 2.—A FEW SELECTED TESTS IN TUBERCULOUS MENINGITIS AND POLIOMYELITIS SHOWING THE USUAL REACTIONS AND THE EXTREME VARIATIONS

Tuberculous meningitis	Poliomyelitis
±± 1 2 4 4 2 ± 0 0	1 1 2 3 3 2 1 0 0 0
±±± 1 3 3 2 ± 0 0 0	1 1 2 3 3 3 1 0 0 0
±±± 2 5 5 5 1 0 0	1 1 1 2 3 2 0 0 0 0
± 1 2 4 4 4 ± 0 0 0	1 1 1 2 3 3 1 0 0 0
± 2 4 4 2 2 ± 0 0 0	1 1 2 2 1 0 0 0 0 0
0 0 0 2 3 3 2 0 0 0	1 1 2 3 2 1 0 0 0 0
0 0 ± 5 5 3 ± 0 0 0	1 2 2 1 0 0 0 0 0 0
0 0 0 3 4 4 4 0 0 0	1 1 2 1 0 0 0 0 0 0
1 1 1 4 4 4 4 1 0 0	

SUMMARY

The colloidal gold reaction with cerebrospinal fluid from patients with poliomyelitis has been recorded in isolated instances, and by one of us in a small number of sporadic cases occurring in St. Louis. The results in these few cases indicated that this reaction might be of service in the diagnosis of this disease. In order further to investigate this point, cerebrospinal fluids from patients in 100 cases occurring in the recent New York epidemic were examined, and it is the object of this paper to record the results.

From these results it is to be concluded that the colloidal gold reaction is of distinct service in the diagnosis of poliomyelitis. The greatest usefulness of the reaction is in showing to be pathologic a fluid which does not give other evidence of abnormality when examined as to its albumin, globulin and cellular content. This evidence of abnormality is most useful in those cases of poliomyelitis in which there are the usual symptoms of onset and in which paralysis has not developed. It is also our belief that the Lange reaction is of service in differentiating between poliomyelitis and tuberculous meningitis, between which diseases there not infrequently arises for a time a confusion as to diagnosis.